

Amendments to the Specification:

Please replace the paragraph beginning on page 7, line 5, with the following amended paragraph:

In general, a preferred zinc finger framework has the structure:

(A) $X_{0-2} C X_{1-5} C X_{9-14} H X_{3-6} H/C$ (SEQ ID NO.:81)

where X is any amino acid, and the numbers in subscript indicate the possible numbers of residues represented by X.

Please replace the paragraph beginning on page 7, line 12, with the following amended paragraph:

In a preferred aspect of the present invention, zinc finger nucleic acid binding motifs may be represented as motifs having the following primary structure:

$X^a C X_{2-4} C X_{2-3} F X^c X X X L X X H X X X^b H$ - linker (SEQ ID NO.:40)

-1 1 2 3 4 5 6 7 8 9

Please replace the paragraph beginning on page 14, line 6, with the following amended paragraph:

Figure 1c shows a phage ELISA binding assay showing discrimination of pyrimidines by representative phage-selected zinc-fingers. The matrix shows three different zinc finger phage clones (x, y and z) reacted with four different DNA binding sites present at a concentration of 3 nM. Binding is represented by vertical bars which indicate the OD obtained by ELISA (Choo and Klug, (1997) Curr. Opin. Str. Biol. 7:117-125). The amino acid sequences (SEQ ID NOS.: 8, 62-64, 7 and d5) of the variant α -helical regions from the selected zinc fingers are: REDVLRHGK (x) (SEQ ID NO.:5), RADALMVHKKR (y) (SEQ ID NO.:6), and RGPDLARHGR (z) (SEQ ID NO.:7). The DNA sequences (SEQ ID NOS.:55, 44 and 43 [[56]]) contain the generic binding site GCGGNGGCG (SEQ ID NO:4) where the central (bold) nucleotide was either: uracil (U), thymine (T), cytosine (C) or 5-methylcytosine (M).

Please replace the paragraph beginning on page 14, line 6, with the following amended paragraph:

Figure 2 shows the effect of cytosine methylation on DNA binding by phage-selected zinc fingers. Graphs show three different zinc finger phage binding to the DNA sequence (SEQ ID NO.:43) GCGGCGGCG in the presence (circle) and absence (triangle) of methylation of the central base (bold). The zinc finger clones tested contained variant α -helical regions of the middle finger as follows: (a) RADALMVHKR (SEQ ID NO.:6), (b) RGPLARHGR (SEQ ID NO.:7) [[4]] and (c) REDVLIRHGK (SEQ ID NO.:5). These respective zinc finger clones preferentially bind their cognate DNA site in the presence, absence, or regardless of cytosine methylation.

Please replace the paragraph beginning on page 15, line 1, with the following amended paragraph:

Figure 6 shows binding of zinc finger polypeptides zfHHA(M) and zfHAE(M) to the nucleotide sequence (Figure 6a) (SEQ ID NO.:80) in response to selective methylation by addition of methylase enzymes (Figure 6b). Polypeptides zfHHA(Y) and zfHAE(Y) do not discriminate between methylated and unmethylated DNA, as expected.

Please replace Table 1 on page 36 with the following amended Table 1:

Table 1

Oligonucleotide Sequences

HAE(M)	5'-tatagtG-GGMC-GGCGgtgcacagtcagtcacacacgtc-3' (SEQ ID NO.:15)
HHA(M)	5'- tatagtG-GMGC-GGCGgtgcacagtcagtcacacacgtc-3' (SEQ ID NO.:16)
HAE(Y)	5'- tatagtG-GGYC-GGCGgtgcacagtcagtcacacacgtc-3' (SEQ ID NO.:17)
HHA(Y)	5'- tatagtG-GYGC-GGCGgtgcacagtcagtcacacacgtc-3' (SEQ ID NO.:18)
HAE(T)	5'- tatagtG-GGTC-GGCGgtgcacagtcagtcacacacgtc-3' (SEQ ID NO.:19)

wherein: M = 5-me
Y = pyrimidine (C/T/M)
R = Purine (A/G)

Zinc Finger Clones

	F1 -1 1 2 3 4 5 6	F2 -1 1 2 3 4 5 6	F3 -1 1 2 3 4 5 6
zfHAE(M)	R S D E L T R (SEQ ID NO.:20)	R S D D L S Q (SEQ ID NO.:25)	R K H H R K E (SEQ ID NO.:30)
zfHHA(M)	R S D E L T R (SEQ ID NO.:21)	R S D D L T R (SEQ ID NO.:26)	Y D G A R K R (SEQ ID NO.:31)
zfHAE(Y)	R S D E L T R (SEQ ID NO.:22)	R S D D L T G (SEQ ID NO.:27)	H N R D R K R (SEQ ID NO.:32)
zfHHA(Y)	R S D E L T R (SEQ ID NO.:23)	R S D H L S A (SEQ ID NO.:28)	T N S T R T K (SEQ ID NO.:33)
zfHAE(T)	R S D E L T R (SEQ ID NO.:24)	R S D D L S T (SEQ ID NO.:29)	R N D H R K T (SEQ ID NO.:34)

Please replace the paragraph beginning on page 41, line 25, with the following amended paragraph:

Thus, a zinc finger which recognises the DNA sequence (SEQ ID NO.:56) GCGGCCGCG selected by phage display as described in Choo, Y. & Klug, A. (1994) Proc. Natl. Acad. Sci. U.S.A. 91:11163-11167. by the method of the preceding examples, a further zinc finger is selected which is capable of binding to the sequences (SEQ ID NO.: 57 [[54]]) GCGGMCGCG where the central base M is 5-meC, and used to construct transcription factors as described in the foregoing.

Please replace the Sequence Listing with the accompanying paper copy of the substitute Sequence Listing, page numbers 1-22.